REMARKS

Claims 1-18, 20-21 and 45-58 were pending. Claims 1-9 have been amended by incorporating the subject matter of claim 12. Claims 12-14 have been canceled. Claim 15 has been amended, which amendment is supported by the originally-filed application (including the claims), for example, claim 12 as previously pending and page 13, lines 2-3 of the earlier priority application USSN 60/408,571. Claims 20 and 51 have been amended by replacing the term "IL 13" with "IL-13" as suggested by the Examiner, which amendments (as well as corresponding amendments to the specification) are merely typographical. Claims 20 and 21 have also been amended, and new claims 59-60 have been added; support for these amendments can be found, for example, at page 12, line 22 – page 13, line 5 of USSN 60/408,571. Accordingly, the claim amendments herein do not introduce any new matter.

Applicant next addresses each outstanding issue raised in the Office Action.

Priority

Applicant notes with appreciation the Examiner's acknowledgment of the effective filing date of claims 1-2 as being 6 September 2002, the filing date of the earlier priority application USSN 60/408,571. However, Applicant respectfully traverses the Examiner's finding that the priority application does not support sufficient written description for certain claim limitations in claims 3-18, 20-21 and 45-58. To expedite prosecution, Applicant has canceled claims 12-14 and 52-58.

As an initial matter, the claims at issue and as amended find full written description support in the present application. The claims also find support in each of the priority applications: USSN 60/408,571, filed on 6 September 2002, and USSN 60/469,189, filed on 9 May 2003.

"The subject matter of [a] claim need not be described literally (using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement." MPEP § 2163.02. The MPEP also cites *Martin v. Johnson*, 424 F.2d 746, 751 (CCPA 1972), which states

that "the description need not be *ipsis verbis* [i.e., in the same words] to be sufficient." MPEP § 2163 (3)(a). Moreover, "[m]ere rephrasing of a passage does not constitute new matter… [and] a rewording of a passage where the same meaning remains intact is permissible." MPEP § 2163.07 (I). Also, while an applicant may not rely on obviousness *per se* as evidence of written description, "[i]nformation which is well known in the art need not be described in detail in the specification." MPEP § 2163 (II)(A)(2).

In accordance with these principles, the priority documents – and particularly USSN 60/408,571 filed on 6 September 2002 – provide ample support for the terms pointed out by the Examiner in the Office Action, as demonstrated in the table below:

Claim No.	**Claim Language**	**Exemplary Support in USSN 60/408,571**
3	reducing the severity of an asthma attack	Page 1, second paragraph, stating that asthma, as well as other Chronic Obstructive Pulmonary Diseases, "are characterized as generalized airways [sic] obstruction," and airway obstruction "is defined as an increased resistance to airflow during forced expiration." Accordingly, severity of an asthma attack can be represented by specific airway resistance. The specification further provides examples demonstrating reduced airway resistance in response to the treatments. *See, e.g.*, Figure 1, 3, 5a, 5b, 6a and 6b. Also at page 16, lines 11-15: "The anti-C5 treatments had inhibited the production of complement component C5 in the cascade, and by inhibiting C5 production, the mice experienced significantly less airway constriction. The positive control group that was treated with a control antibody showed increased specific airway resistance caused by an asthmatic attack." *See also*, page 19, lines 2-4.
4	reducing airway obstruction in a subject	As noted above, the specification teaches that airway obstruction "is defined as an increased resistance to airflow during forced expiration" and provides the pertinent examples.
5	increasing air flow in a subject	Page 17, lines 13-15: "The anti-C5 antibody had inhibited inflammatory response of the complement components, and allowed greater air passage during the asthma attacks . . . ."
6	reducing bronchial spasm in a subject	Page 1, lines 20-21: "Asthmatic airway obstruction typically results from bronchospasms." As noted above, the specification teaches that airway obstruction is manifested in an asthma attack and the severity can be reduced with the anti-C5 antibody

		treatments.
7	treating a chronic obstructive pulmonary disease	Page 1, second paragraph, stating that asthma is known as a Chronic Obstructive Pulmonary Disease.
8	having established airway inflammation	Page 3, the two full paragraphs, describing the two phases to an allergic asthma attack and that airway inflammation is present in subjects having asthma attacks. Page 15, the full paragraph (Example 1) also describes the two phases in the mouse model.
9	effective bronchial-dilating amount of an anti-C5 antibody	Page 16, lines 11-13: "The anti-C5 treatments had inhibited the production of complement component C5 in the cascade, and by inhibiting C5 production, the mice experienced significantly less airway constriction."
45-50	nebulization	*See* Example 3 (page 17, line 16 – page 19, line 6) and more specifically, page 18, lines 15-18, stating that the anti-C5 antibody was "administered to the test animals through nebulization . . . ."
20, 51	combination therapy with all of [the] members recited in the claims 20 and 51	*See* page 4, lines 12-14 (discussing combination therapy). The specific members recited in the claims were well known in the art at the time of the filing date (6 September 2002).
21	without substantially reducing systemic complement activity in a subject	Page 19, lines 2-5: "Specifically, although both aerosol and intravenous administration were effective at reducing the severity of an asthma attack, the aerosol administration did so without substantially reducing systemic C5 activity."

Claim Objections

Applicant has amended the claims at issue (claims 20 and 51) and the corresponding text in the specification as suggested by the Examiner.

Rejection under 35 USC § 112, Second Paragraph

While not conceding to any aspect of the Examiner's stated reasons for this rejection, Applicant has amended claim 15 and canceled claims 55-58 to expedite prosecution.

Rejection under 35 USC § 112, First Paragraph (Enablement)

While not conceding to any aspect of the Examiner's stated reasons for this rejection, Applicant has amended the claims at issue, and canceled claims 12-14 and 57 to expedite prosecution.

Rejection under 35 USC § 112, First Paragraph (Written Description)

Claims 52-58 are rejected as allegedly lacking adequate written description, particularly with respect to the term "compounds." While Applicant does not concede to any aspect of the Examiner's stated reasons for rejection, claims 52-58 have been cancelled herein, which action obviates their rejections.

Rejection under 35 USC § 102(e)

Claims 1-18, 20-21 and 45-58 are rejected as allegedly being anticipated by Krause et al. (US 2004/0014782). Applicant respectfully traverses.

First, the claimed invention had been conceived prior to the effective filing date of the Krause et al. reference. To demonstrate that, Applicant files concurrently herewith an executed Declaration by the inventor under 37 C.F.R. § 1.131. As detailed in the Declaration, the inventor had conceived of the invention by 20 December 2001 or earlier, as indicated by the dated experimental plans on evaluating the efficacy of anti-C5 antibody BB5.1 using an asthma mouse model. As demonstrated by Examples 1-3 of the priority application, USSN 60/408,571 (filed on 6 September 2002), the inventor performed the animal studies as planned.

Thus the Declaration establishes that Applicant conceived of the invention prior to 29 March 2002, the filing date of the priority application of Krause and was diligent from prior to 29 March 2002 to at least 6 September 2002. Applicant further reserves the right to provide evidence of an even earlier date of conception. Accordingly, Krause cannot serve as a 102(e) reference against the instant application, and reconsideration and withdrawal of this rejection are respectfully requested.

Applicant's submission of the antedating Declaration is, however, in no way a concession to the reasons stated in the Office Action underlying the rejections based on Krause. Assuming *arguendo* that, Krause were prior art against the instant application, Applicant provides the following remarks in support of patentability of the instant claims.

The instant claims are drawn to methods for treating chronic obstructive pulmonary diseases such as asthma by administering to a subject having the disease(s) a compound that inhibits complement activation, such as an anti-C5 antibody that blocks the conversion of C5 into C5a and C5b.

Krause et al. discloses a genus of small molecule C5a receptor inhibitors for use in treating inflammation including disorders such as rheumatoid arthritis, skin injuries, infections, and lung diseases such as asthma. According to the Office Action, Krause et al. anticipates the instant claims because it "teach[es] the use of C5a antagonists, including anti-C5 antibodies …in the treat[ment of] respiratory diseases [and] lung disorders, including ARDS and asthma . . . ." Applicant respectfully disagrees for at least two reasons: ***first***, the C5a antagonists disclosed by Krause do not include anti-C5 antibodies; ***second***, the reference does not disclose methods or kits including anti-C5 antibodies for use in treating respiratory disorders.

a. The "C5a Antagonists" of Krause do not include anti-C5 antibodies.

At paragraphs [0035] and [0036], Krause defines two types of active agents that can be used for treating inflammation in accordance with its disclosure: "C5a antagonists" (or "C5a receptor antagonists") and "C5a receptor-inactive therapeutic agents." The "C5a antagonist," according to

the reference, is "any compound that exhibits C5a antagonist activity within the a [sic] C5a receptor-mediated chemotaxis, radioligand binding assay, or calcium mobilization assay as provided [in the reference]." Krause et al. at page 3, paragraph [0035]. The reference further provides examples of numerous small molecule C5a antagonists and clarifies the nature of the three assays which are used to determine if a compound meets the definition of "C5a antagonist." *Id.* at pages 4 to 17, paragraphs [0040] to [0198]. Notably, in the nearly 14 full pages of C5a antagonists disclosed in Krause, there is not one mention of an anti-C5 antibody being a member of this genus.

To the contrary, anti-C5 antibodies are recited but two times in Krause, each time narrowly under the heading of "C5a receptor-inactive therapeutic agent," and, as elaborated on below, only in conjunction with treating rheumatoid arthritis. *See, e.g.*, Krause at page 18, paragraphs [0206] and [0207] (stating that "at least one C5a receptor-inactive therapeutic agent is … an anti-C5 monoclonal antibody"). "C5a receptor-inactive therapeutic agents" are defined in the reference as any therapeutic agent that is not a C5a antagonist. *Id.* at page 4, paragraph [0036].

Thus, contrary to the Office Action's interpretation of the reference, Krause's genus of C5a antagonists does not include anti-C5 antibodies. In fact, the reference teachings – namely: that anti-C5 antibodies are not C5a antagonists – are actually diametrically opposite of the interpretation asserted by the Office Action.

b. The Krause asthma-related methods and kits do not include anti-C5 antibodies.

The second assertion by the Office Action is that Krause discloses methods and/or kits including anti-C5 antibodies for use in treating respiratory disorders. With this position, Applicant also respectfully disagrees.

In the section of its disclosure titled "Combination Therapy," Krause discloses in a distinct and modular way specific combination therapies useful for treating different types of inflammation. That is, in each therapeutic "module" related to the treatment of a specific inflammatory condition (e.g., rheumatoid arthritis), Krause provides a number of specific C5a receptor-inactive therapeutic

agents that can be used in combination with the C5a receptor antagonists of its disclosure. For example, at pages 17 and 18, Krause discloses a combination therapy for treating rheumatoid arthritis, which therapy includes "at least one C5a antagonist and a C5a receptor-inactive agent that is an anti-arthritic agent (i.e., a C5a receptor-inactive anti-arthritic agent)." *Id.* at page 17, paragraph [0202] (emphasis added). In another therapeutic module, Krause provides a combination therapy for treating lung disorders using at least one C5a antagonist and a C5a receptor-inactive agent "useful in the treatment of asthma." *Id.* at page 18, paragraph [0227] and 23, paragraph [0279].

Only twice are anti-C5 antibodies (at paragraphs [0207] and [0277]) recited in Krause, and in each instance only in "rheumatoid arthritis" modules and only as one of a laundry list of well-known, potential C5a receptor-inactive anti-arthritic agents such as, e.g., NSAIDs, COX inhibitors, anti-TNF agents, anti-IL-1 agents, and anti-CD20 agents, useful for treating rheumatoid arthritis. Notably, at the effective date of Krause, Alexion Pharmaceuticals, Inc. was engaged in a well-known phase II clinical trial evaluating an anti-C5 antibody in rheumatoid arthritis. *See, e.g.*, PR Newswire article dated 4 August 1999 and Abstract of Kaplan (2002) Curr Opin Investig Drugs 3(7):1017-1023 (stating that - "Eculizumab … is under development by Alexion as a potential treatment for … rheumatoid arthritis (RA) … In January 2002, a phase IIb trial was initiated for RA").

In contrast, the two therapeutic modules drawn to treating lung disorders – at pages 18, 19, and 23 of Krause – are devoid of any mention of anti-C5 antibodies, let alone as being one of the C5a receptor-inactive agents useful for treating asthma. Instead, the lung disorder-related therapeutic modules recite a lung disorder-specific laundry list of well-known asthma treatments including, e.g., anti-thrombin agents, beta adrenergic receptor agonists, and corticosteroids. Krause et al. at pages 18-19, paragraphs [0227] to [0229]. To be clear: there is no disclosure or even a suggestion in Krause of the use of an anti-C5 antibody, either alone or in combination with a C5a antagonist, for the treatment of a lung disorder such as asthma, despite the fact that anti-C5 antibodies had been known in the art. Rather, as discussed above, Krause teaches that an anti-C5

antibody is not a C5a antagonist and does not include such antibodies, even as a supplemental agent, in its asthma-related therapeutic modules.

In view of the foregoing, it is clear that anti-C5 antibodies are not part of the genus of C5a antagonists recited in Krause. Moreover, it is clear that neither the asthma-related methods nor kits disclosed in Krause feature an anti-C5 antibody, as instantly claimed. Accordingly, the instant claims are not anticipated by Krause and Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102.

Rejection under 35 USC § 103(a)

Applicant maintains that Krause is not properly 102(e) prior art against the instant application. In the alternative, assuming *arguendo* that, Krause could serve as a prior art against the instant application, Applicant maintains that Krause does not teach or suggest an anti-C5 antibody, in asthma-related methods and compositions. The secondary references are directed to methods and compositions suitable for nasal inhalation, but none of them cures the deficiency of Krause *vis-a-vis* the instant claims. Accordingly, Applicant respectfully requests reconsideration and withdrawal of this rejection.

Provisional Rejection under Obviousness-type Double Patenting

Claims 1-18, 20-21 and 45-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-45 of copending application USSN 11/127,438. Applicant requests that the Examiner hold the provisional double patenting rejection in abeyance until otherwise allowable subject matter is identified in the instant application. Once allowable subject matter has been identified, Applicant will evaluate providing arguments or filing a terminal disclaimer in view of the claims pending at that time.

In view of the above amendments and remarks, Applicant believes that the pending application is in condition for allowance, which action is respectfully requested.

Applicant believes that no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. ALXN-P01-102 from which the undersigned is authorized to draw.

Dated: January 25, 2011

Respectfully submitted,

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